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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
RAWLINGS, STEPHEN L	
ART UNIT	**PAPER NUMBER**
1643	

DATE MAILED: 09/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/848,948	HANASH ET AL.	
	Examiner	Art Unit	
	Stephen L. Rawlings, Ph.D.	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 July 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6-14 and 16-34* is/are pending in the application.

4a) Of the above claim(s) *6-13 and 19-33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,14,16-18 and 34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 September 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on July 8, 2005 has been entered.

1. The amendment filed July 8, 2005 is acknowledged and has been entered. Claims 5 and 15 have been canceled. Claims 1, 2, and 14 have been amended. Claims 33 and 34 have been added.

2. Claims 1-4, 6-14, and 16-34 are pending in the application. Claims 6-13 and 19-33 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a non-elected invention or species of invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in paper filed January 21, 2003 (Paper No. 7).

3. Claims 1-4, 14, 16-18, and 34 are currently subject to examination.

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Election/Restrictions

5. Newly submitted claim 33 is directed to an invention that is independent or distinct from the invention originally claimed for the following reasons:

Newly added claim 33 is directed to a method for diagnosing breast or colon cancer. Applicant elected the species of the inventions of Groups I-XIV (following their rejoinder),

where said cancer is lung cancer. Accordingly, claim 33 is drawn to the subject matter of a non-elected species of invention.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim 33 has been withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Grounds of Rejection Withdrawn

6. Unless specifically reiterated below, Applicant's amendment filed July 8, 2005 has obviated or rendered moot the grounds of rejection set forth in the Office action mailed February 8, 2005.

Grounds of Rejection Maintained

Claim Rejections - 35 USC § 102

7. The rejection of claims 14 and 34 under 35 U.S.C. 102(a) as being anticipated by Newton et al. (*J. Immunol.* 1998; **160**: 1427-1435) is maintained.

At pages 9 and 10 of the amendment filed July 8, 2005 Applicant has traversed this ground of rejection.

Applicant's argument has been carefully considered but not found persuasive for the following reasons:

Although Applicant has correctly remarked that the prior art does not teach diagnosing cancer by a process comprising detecting S100-A7 or S100-A8, the claims are drawn to a kit comprising a component for detecting the presence of the S100 proteins, S100-A7 or S100-A8 in a biological sample, wherein said component is an anti-S100 antibody. Accordingly, the claims are directed to a kit comprising an anti-S100 antibody. The prior art teaches a commercially available, prepackaged "kit" comprising an antibody that binds an S100 protein.

If the preamble and its recitation that the component of the kit is intended for use in detecting the presence of S100-A7 or S100-A8 were considered, *arguendo*, "necessary to give life, meaning and vitality to the claim" (*Pitney Bowes Inc. v. Hewlett-Packard Co.*, 51 USPQ2d 1161, 1165-66 (CA FC 1999); *Kropa V. Robie* 88 USPQ 478, 480-481 (CCPA 1951)) and

thereby materially or functionally limit the claimed subject matter, it is duly noted that an anti-S100 antibody of which the kit is comprised may in fact be used to detect the presence of S100-A8 or S100-A9 in a biological sample, because the antibody either binds one of these two proteins or it binds another member of the S100 family of proteins, in which case it is used to distinguish such other members from S100-A8 or S100-A9 to facilitate identification and therefore detection of the latter.

Double Patenting

8. The provisional rejection of claims 14, 16-18, and 34 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 13-15 of copending U.S. Patent Application No. 10/461,424 in view of BIO-RAD Life Sciences Research Products Price List Q (March 1991; pages 190 and 233-240) is maintained.

This is a provisional obviousness-type double patenting rejection.

At page 11 of the amendment filed July 8, 2005 Applicant has stated that a terminal disclaimer will be filed to overcome this ground of rejection upon notification of allowable claims.

New Grounds of Objection

Specification

9. The abstract of the disclosure is objected to because it is entitled "Abstract of the Invention", where is should be entitled "Abstract" or "Abstract of the Disclosure". Correction is required. See MPEP § 608.01(b).

New Grounds of Rejection

Claim Rejections - 35 USC § 102

10. Claims 1 and 2 are rejected under 35 U.S.C. 102(b) as being anticipated by Celis et al. (*J. Urol.* 1996 Jun; **155** (6): 2105-2112).

Claims 1 and 2 are drawn to a method for diagnosing bladder cancer in a subject comprising detecting S100-A7 in a urine sample from a subject using an immunoassay and comparing the level of the protein to the level of the protein in a control sample, wherein a

relative increase in the level of the protein in the sample of urine is an indicator that the subject of a subject with bladder cancer.

Celis et al. teaches detecting S100-A7 in a urine sample from a subject using an immunoassay and comparing the level of the protein to the level of the protein in a control sample, wherein a relative increase in the level of the protein in the sample of urine is an indicator that the subject of a subject with bladder cancer; see entire document (e.g., the abstract; page 2106, column 1, through page 2107, column 1; page 2108, column 1, through page 2109, column 1).

Claim Rejections - 35 USC § 103

11. Claims 3, 14, 16-18, and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Celis et al. (*J. Urol.* 1996 Jun; **155** (6): 2105-2112) in view of BIO-RAD Life Sciences Research Products Price List Q (March 1991), pages 190 and 233-240 (of record).

Claim 3 is drawn to a method for diagnosing bladder cancer in a subject comprising detecting S100-A7 in a urine sample from a subject using an immunoprecipitation assay and comparing the level of the protein to the level of the protein in a control sample, wherein a relative increase in the level of the protein in the sample of urine is an indicator that the subject of a subject with bladder cancer.

Claims 14, 16-18, and 34 are drawn to a kit comprising an anti-S-100 antibody (claims 14 and 34), wherein the antibody is radioactively, fluorescently, colorimertrically, or enzymatically labeled (claims 16 and 17) or wherein the kit further comprises a labeled secondary antibody that immunospecifically binds the anti-S100 antibody (claim 18).

Celis et al. teaches that which is set forth above in the rejection of claims 1 and 2 under 35 U.S.C. § 102. In addition, Celis et al. teaches a labeled secondary antibody that binds immunospecifically to the disclosed anti-S100 antibody (page 2107, column 1).

However, Celis et al. does not expressly teach a kit comprising an anti-S100 antibody that is detectably labeled, nor does Celis et al. expressly teach detecting S100-A7 using an immunoprecipitation assay.

BIO-RAD Life Sciences Research Products Price List Q (March 1991) discloses that which is set forth in the preceding Office actions (e.g., section 12, beginning at page 7 of the Office action mailed May 11, 2004).

It would have been *prima facie* obvious to one ordinarily skilled in the art at the time of the invention to detect S100-A7 in the biological samples, as disclosed by Celis et al., but using an immunoprecipitation assay, as opposed to or in addition to the other specifically disclosed immunoassays, because as taught by BIO-RAD Life Sciences Research Products Price List Q (March 1991), it was routine and conventional at the time of the invention to detect and/or quantify a protein by immunoprecipitation. In addition, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of invention to manufacture a kit comprising reagents for detecting S100-A7 and to use it for the diagnosis of bladder cancer. Moreover, it would have been obvious to include in such a kit a detectably labeled antibody (e.g., a fluorescently labeled antibody) that binds S100-A7 or alternatively a detectably labeled secondary antibody that bind the anti-S100-A7 antibody, because Celis et al. teaches, for example, such a fluorescently labeled secondary antibody is used in performing immunocytochemical analyses, and, as taught by BIO-RAD Life Sciences Research Products Price List Q (March 1991), it was routine and conventional to detectably label the antibody used to immunoprecipitate a protein to which the antibody binds in the process of detecting and/or quantifying the protein by immunoprecipitation and other immunoassays; and as further taught by BIO-RAD Life Sciences Research Products Price List Q (March 1991), it was routine and conventional at the time of invention to manufacture and use kits comprising reagents used in the same process. One of ordinary skill in the art at the time of the invention would have been motivated to do so, because kits provide ease and convenience and Celis et al. teaches detecting and/or quantifying S100-A7 in the urine of a subject is an indicator of a subject with bladder with cancer, where the relative abundance of the protein is greater than that in controls.

Claim Rejections - 35 USC § 112

12. Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, because the specification, **while being enabling for** a process for diagnosing bladder cancer in a subject comprising detecting S100-A7 in a urine sample from a subject using an immunoassay and comparing the

level of the protein to the level of the protein in a control sample, wherein a relative increase in the level of the protein in the sample of urine is an indicator that the subject of a subject with bladder cancer, **does not reasonably provide enablement for** a process for diagnosing *any type of cancer* by detecting the presence and/or relative abundance of S100-A7 in a sample of *any biological fluid.* The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The amount of guidance, direction, and exemplification disclosed in the specification, as filed, would not be sufficient to enable the skilled artisan to use the claimed invention at the time the application was filed without undue experimentation.

MPEP § 2164.01 states:

> The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916) which postured the question: is the experimentation needed to practice the invention undue or unreasonable? That standard is still the one to be applied. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). Accordingly, even though the statute does not use the term "undue experimentation," it has been interpreted to require that the claimed invention be enabled so that any person skilled in the art can make and use the invention without undue experimentation. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors, which have been outlined in the Federal Circuit decision of *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), include, but are not limited to, the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed. See also *Ex parte Forman*, 230 USPQ 546 (BPAI 1986).

The prior art (e.g., Celis et al.; cited supra) teaches a process for diagnosing bladder cancer in a subject comprising detecting S100-A7 in a urine sample from a subject using an immunoassay and comparing the level of the protein to the level of the protein in a control

sample, wherein a relative increase in the level of the protein in the sample of urine is an indicator that the subject of a subject with bladder cancer.

Although Celis et al. discloses a relative abundance of S100-A7 in the urine of patients with bladder cancer, Celis et al. teaches the protein could not be detected in serum (e.g., page 2109, column 1).

The specification provides very little guidance, direction, and exemplification with regard to the claimed invention. At page 10, lines 13-15, the specification teaches, "S100-A7 and S100-A8 proteins were shown to be secreted by breast cancer cells, which provide the basis for diagnostic and prognostic assays for breast cancer" and at page 17, lines 16 and 17, the specification discloses, "mass spectrometry identified S100A7 as a secreted protein in breast cancer". However, apart from this very little guidance and direction, there is none other that would enable the artisan to practice the claimed invention and moreover, the use of the claimed invention to diagnose any type of cancer, including breast cancer has not been exemplified.

As evidenced by Celis et al., the skilled artisan cannot predict which types of cancer cells secrete S100-A7 into the various different biological fluids (e.g., serum, plasma, urine, saliva, cerebrospinal fluid, feces, etc.).

Accordingly, the claimed invention could not be used without undue and unreasonable experimentation, as it would be first be necessary to determine which types of cancer secrete detectable levels of S100-A17 into which types of biological fluid and then whether or not the levels of the protein in these fluids is substantially different from the levels found in such fluids acquired from unaffected control individuals, such that a difference would provide an indication of a subject with cancer.

In conclusion, upon careful consideration of the factors used to determine whether undue experimentation is required, in accordance with the Federal Circuit decision of *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the amount of guidance, direction, and exemplification disclosed in the specification, as filed, is not deemed sufficient to have enable the skilled artisan to use the claimed invention at the time the application was filed without undue and/or unreasonable experimentation.

Conclusion

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen L. Rawlings, Ph.D. whose telephone number is (571) 272-0836. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, Ph.D. can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Stephen L. Rawlings, Ph.D.
Examiner
Art Unit 1643

slr
September 9, 2005